UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/129,758	08/05/1998	RAINER WALDMANN	1099-00	5113

35811 7590 11/29/2006

IP GROUP OF DLA PIPER US LLP
ONE LIBERTY PLACE
1650 MARKET ST, SUITE 4900
PHILADELPHIA, PA 19103

EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	Application No.	Applicant(s)	
	09/129,758	WALDMANN ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/24/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11-13,15,17-23,26,27,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11-13,15,17-23,26,27,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed 8/24/06 has been entered. Applicant has amended claims 1 and 11. Applicant has also added new claims 30-31. Claims 1, 11-13, 15, 17-23, 26-27 and 30-31are pending and will be examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is rejected because it is not clear what is "comprising an amino acid sequence selected **in** the group consisting of". It is suggested to overcome the rejection the claim be amended to read "comprising the amino acid sequence **from** the group consisting of"

Claim 31 is rejected as being indefinite because method requires "wherein the transformed cell expresses the mammalian neuronal ASIC cationic channels" and then states "the amino acid sequence of which is selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:8". The limitation "wherein the transformed cell expresses the mammalian neuronal ASIC cationic channels" infers that more than one channel is expressed. The limitation "the amino acid sequence of which is selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:8" infers that there is a choice as to which ASIC cationic channels are expressed. Since at least two ASIC cationic channels are required by the method the Markush group must contain more than two members for a selection to be made. It is suggested to overcome the rejection the claim be amended to "The method according to claim 22, wherein the transformed cell expresses the

mammalian neuronal ASIC cationic channels having the amino acid sequence of SEQ ID NO:2 and SEQ ID NO:8."

4. Claims 1, 11-13, 15, 17-23, 26-27, 30-31 are rejected under 35 U.S.C. 101. Claims 1, 11-13, 15, 17-23, 26-27 remain rejected under 35 U.S.C. 101, for reason of record in the previous Office Action, and those given below, because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Newly added claims 30 and 31 are rejected under 35 U.S.C. 101, for the same reasons as those of claims 1, 11-13, 15, 17-23, 26-27 (of record in the previous Office Action, and those given below), because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Applicants arguments pertaining to the rejection of claims 1, 11-13, 15, 17-23, 26-27 under 35 U.S.C. 101 and 112, first paragraph are summarized below:

Applicants argue that the application clearly teaches: a) the link between ASIC channels and ischemia, b) ASIC channels and pain perception, c) ASIC channels are implicated in neurodegeneration, and d) that ASIC channel blockers are drugs that can be used to limit postischemic neuronal death. Applicant's arguments have been fully considered but they are not found persuasive. Applicants have previously argued that ASIC channels are expressed throughout the brain, conduct the flux of ions through the membranes of cells. The family of ion channel proteins is responsible for a number of specific cellular activities including the propagation of nerve impulses and a number of neurodegenerative diseases. ASIC channels are activated by extracellular acidification and associated with a number of activities (nociception, taste transduction, anxiety disorder, pathaologies such as cerebral neuronal degeneration), and these activities can readily be used by those skilled in the art. Applicants' arguments have been fully considered but are not found persuasive. The general activity of ion transport, possessed by the family of channel proteins, cannot be used to support utility in instant case. A detailed argument to Applicants' traversal is provided below.

In light of the specification, the skilled artisan can conclude that the protein of instant invention is a cationic channel protein. However, no disclosure is provided within

the instant specification on what specific function the claimed cationic channel protein possesses, nor are any disease states disclosed that are directly related to the claimed channel dysfunction. A detailed argument to Applicants' traversal is provided below.

The references supplied by applicants clearly show that the role of ASIC protein channels was unknown at the time of filing of instant application. For example, see Chen et al (Proc. Natl. Acad. Sci. USA, Vol. 95, pp10240-10245, August 1998), page 10245, column 1, last paragraph, which states ASIC channels have a widespread distribution in the central nervous system but as yet have an unknown physiological role.

Allen at al (J. of Physiology, Vol 543 (2), pages 521-529, 2002), page 521, column 2, discloses that little is known about the modulation of ASIC channels in the central neurons, ASIC channels require a large and rapid fall of pH to be activated and it is unclear when this might happen in the CNS.

Wemmie et al (The Journal of Neuroscience, Vol. 23, (13) pages 5496-5502, 2003) page 5502, column1 discloses that additional studies will be necessary to delineate the multiple possible effects of ASIC on behavior.

Baron et al (Journal of Physiology, Vol 539(2), pages 485-494, 2002) page 485 discloses that ASIC are functionally diverse and the role of ASIC1a, ASICa, ASIC2b and ASIC4 in the central neurons remains to be established. Therefore, based on the art and the specification, the role of the claimed channel and its association with a specific disease or dysfunction was unknown at the time of filing of instant application.

Although the family of ASIC proteins domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. No disease states are disclosed that are directly related to claimed channel dysfunction. The specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polypeptide/nucleic acid or methods of its use. The specification provides a laundry list of diseases that may be associated with claimed invention but does not provide any data or nexus between the claimed invention and stated use.

The claimed invention belongs to a family of ion transporting proteins, which have different electrophysiological properties and divergent physiological functions that result from the transport of said ions. The gated channels are a complex family of ion channel proteins with varied properties and functions (discussed in office Action, 11/17/03. The observation that the claimed invention is an amiloride-sensitive degenerine sodium channel and the disclosure of amiloride sensitivity and certain biophysical properties does not provide support for either a specific and substantial asserted utility or a well-established utility. The specification discloses, pages 2 and 3, the family of structural relatives of ASIC channels (also designated as MDEG) have different electrophysiological properties and that no normal physiological function of said MDEG was known until the demonstration of its activation by protons (also see page 17, lines 13-16). Also disclosed, page 5, inactivation and kinetics and the ionic selectivity of the channel formed after co-expression of different MDEG are different than those if only one channel is expressed. Therefore, expression of the various MDEGs in different tissues may have divergent functional effects due the presence of other channel proteins. The specification, page 5, lines 8-9 states, when referring to claimed ion channel, this property is very similar to that of the proton-activated cationic channel which is implicated in the prolonged sensation of pain caused by acidosis. It is very probable that DRASIC and MDEG2 are part of this channel. The claimed ion channel is speculated to be similar to the family of proton-activated ion channels, but there is no disclosure in the specification as to the relationship of claimed invention to ischemia, pain perception, neurodegeneration, and which known ASIC channel blockers can be used to limit postischemic neuronal death. For example, would activating the claimed channel increase neurodegeneration or decrease it? The specification provides no answers.

All members of the ASIC family do not have the same electrophysiological properties (ASIC2b, does not respond to low pH, ASIC4 is inactive by itself and hence is not thought to encode a proton-gated ion channel), and members have been proposed to function in a wide variety of disease states e.g. pain sensation, ischemia, epilepsy, neurodegenerative diseases, but their role in the brain in is obscure, see Berdiev et al in

previous Office Action, Ref U, page 15023, second column. The function of these channels in the glia remains a mystery; see Berdiev et al, page 15023. Further it has been shown that constitutive amiloride-sensitive currents are a specific feature of the more aggressive brain tumors (see Berdiev et al, page 15034, column 1). Further, amiloride sensitivity cannot be used to infer a specific or well-established utility. Berdiev discloses the difficulty of assigning a function based on amiloride sensitivity. Berdiev, states (page 15034, column 1, second paragraph), "amiloride-sensitive sodium channels cannot easily be classified based on simple biophysical parameters, such as single channel conductance and/or sensitivity to amiloride. This class of ion channel, both in the brain and in epithelial tissues, appear to have a variable composition, and hence tissue-specific differences in biophysical parameters may result from different channel compositions in different tissues". Further the specification provides no significance of the function of amiloride (a drug that blocks sodium/proton antiport and has been used clinically as a potassium sparing diuretic) as it correlates to it role in pain sensation.

The utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the ion channel of the instant invention. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants claimed invention is incomplete. In light of the specification the skilled artisan can conclude that protein of instant invention is a cationic channel protein. However, no disclosure is provided within the instant specification on what specific function the claimed cationic channel protein possesses, nor are any disease states disclosed that are directly related to cation channel dysfunction. Ions are known to play a role of first or second messenger in numerous cellular signaling contexts, but it is not known what role claimed cationic channel plays in signaling and what would be the use of interfering with its function, apart from as targets for drug discovery. Further it is not clear from the

specification if the channel protein disclosed by the amino acid sequence of SEQ ID NO: 4 encoded by SEQ ID NO: 3 has ion transport activity. There is no disclosure in the specification, which shows the protein of SEQ ID NO: 4 was assayed for activity.

The utilities asserted by Applicant are not specific or substantial. Since no specific function of claimed cation channel is known, and the ability to transport ions with no associated function is not considered a well established utility, the hypothesized functions are based entirely on conjecture from homologous polypeptides. The asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record discloses any compounds that treat a specific disorder associated with dysfunction of the nucleic acid of SEQ ID NO: 1, 3 or 8 or its encoded protein (SEQ ID NO: 2, 4 or 8). Similarly, neither the specification nor the art of record discloses any instances where disorders can be affected by interfering with the activity of claimed cation channel. Thus the corresponding asserted utilities are essentially methods of using the claimed cation channel to identify or treat disease states associated with cation channel polypeptide dysfunction and as targets for drug discovery. Therefore, the asserted utilities are essentially methods of testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating or testing for compounds that interact with the claimed cation channel, which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a real world context of use for the claimed cation channel, further experimentation is necessary to attribute a utility to the claimed cation channel. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are Auseful≅ to the chemical arts when this term is given its broadest

interpretation. However, the court held that this broad interpretation was not the intended definition of useful as it appears in 35 U.S.C. 101, which requires that an invention must have either an immediately apparent or fully disclosed real world utility. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The DNA of the instant invention and the protein encoded thereby are compounds, which share some structural similarity to other ion channel proteins based on sequence similarity. The family of proteins related to instant invention may have diverse effects and bind a diverse number of ligands (e.g. syntax , see Berdiev et al). Although the family of ASIC proteins domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. The specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polynucleotides/polypeptides. Also, the specification does not predict whether the claimed polynucleotides/polypeptides would be over expressed or under expressed in a specific, diseased tissue compared to the healthy tissue control. The specification contains assertions that the claimed polynucleotides/polypeptides can be used the art for drug development. However, without a disclosure of a particular disease state in which the claimed polynucleotides/polypeptides are expressed at an altered level or form, it would be impossible to determine what the results of a gene expression/protein expression monitoring assay mean. For example, if a compound is tested on a microarray comprising the claimed polynucleotides and affects expression of the polynucleotides negatively, it cannot be determined if that means that the compound is a potential good drug for a disease or would acerbate the disease if administered. The

test results also would not have meaning in terms of what specific disease is relevant. Further, before the claimed invention can have utility in gene expression, significant, further research would have to be conducted to determine which diseases correlate with altered forms or levels of the claimed polynucleotides, and whether the claimed polynucleotides are over expressed or under expressed in the diseased tissue. The disease state itself has to be identified.

The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids/polypeptides. Even if the expression of Applicants individual polynucleotides/polypeptides are affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotides have no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this nucleic acid could be put.

If a molecule is to be used as a surrogate for a disease state (e.g. gene therapy), some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). In instant case Applicants implicate Alzheimer's disease. Is claimed DNA/protein over-expressed or under expressed in Alzheimer's disease? There is no data in the specification or prior art that provides support for the claimed ion channel dysfunction resulting in Alzheimer's disease. Evidence of a differential expression might serve as a basis for use of the claimed polynucleotides as diagnostics/treatment for diseases. However, in the absence of any disclosed relationship between the claimed polynucleotides or the proteins that are encoded thereby to any disease or disorder and the lack of any correlation with any known disease or disorder, the use of ASIC gene, or its encoded

polypeptide, in therapy, would only serve as the basis for further research. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The ASCI family is functionally highly diverse. When there is great functional diversity in a structurally related class of compounds, the class cannot be used to predict a utility for a new compound that fits in the class by structural similarity. Such is the case here. The specification has not disclosed a specific disease or disorder of any type wherein the claimed polynucleotides/polypeptides are expressed at altered amounts or forms relative to the required control healthy tissue. Significant further research would be required of the skilled artisan to identify such a disease or disorder. Therefore the asserted utility is not substantial. The polypeptide encoded by the polynucleotide belongs to a family in which the members have divergent functions based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family. Although the ASIC belongs to a family of proteins that transport ions, the family has divergent functional effects as consequence of that ion transport, and cannot be compared to the ligase family of proteins, which have a specific effect, ligate DNA.

5. Claims 1, 11-13, 15, 17-23, 26-27 and 30-31 are rejected under 35 U.S.C. 1 12. Claims 1, 11-13, 15, 17-23, 26-27 remain rejected under 35 U.S.C. 1 12, first paragraph for reason of record in the previous Office Action and those given above. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons, one skilled in the

art clearly would not know how to use the claimed invention. Newly added claims 30 and 31 are rejected under 35 U.S.C. 1 12, first paragraph, for the same reasons as those of claims 1, 11-13, 15, 17-23, 26-27 (of record in the previous Office Action, and those given above) because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention.

6. No claim is allowed

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nirmal S. Basi
Art Unit 1646
11/22/06

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600